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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,109	03/04/2002	Rosa Maria Perez Gomariz	G80-016 CIP	5154

21706 7590 06/22/2004

NOTARO AND MICHALOS
100 DUTCH HILL ROAD
SUITE 110
ORANGEBURG, NY 10962-2100

EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,109	PEREZ GOMARIZ ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *2-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/22/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/446,352* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *6/2/2004* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: Raw sequence listing error report

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on March 17, 2004 has been entered. The claims pending in this application are claims 1-6 with claims 2-6 withdrawn from consideration as the result of restriction requirement. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on March 17, 2004.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. For example, see the specification, page 7, third paragraph. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Note that applicant does not address this issue.

Specification

3. The substitute specification filed on March 17, 2004 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because applicant does not provide a substitute specification in clean form without markings.

4. Although applicant submits a substitute specification on March 17, 2004 and intends to overcome the objection below, since the substitute specification has been entered due to the reason above, the following objection is maintained.

The disclosure is objected to because of the following informalities: (1) applicant claims priority for parent case 09/446,352 in the first sentence of the specification. Since the case 09/446,352 now is US Patent No.6,429,188 B1, applicant is required to update the status of the case 09/446,352 in the first sentence of the specification; and (2) at page 13 of specification, there is provided description for Figure 8. Upon reviewing the figures, however, there are Figures 8A-8D. Each figure, e.g. 8A, is considered to be a separate figure and needs to be described in the specification.

This objection can be overcome after applicant provides a substitute specification in clean form so that the substitute specification filed on March 17, 2004 can be entered.

5. The disclosure is objected to because of the following informality: there are no sequencing ID NO for nucleotide sequences in pages 16 and 17, and two amino acid sequences in page 20. This objection can be overcome after applicant provides a substitute specification in clean form so that the substitute specification filed on March 17, 2004 can be entered.

Appropriate correction is required.

Sequencing listing

6. The examiner notes that applicant amends both paper copy of "Sequencing Listing" and copy of "Sequencing Listing" in computer readable form on March 17, 2004. However, the amended sequencing listing in computer readable form fails to comply with the requirements of

37 CFR 1.822 and/or 1.823 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Fishbein *et al.,* (Peptides, 15, 95-100, 1994).

Fishbein *et al.,* teach a chimeric VIP-PACAP analogue but not VIP pseudopeptides function as VIP receptor antagonists. Since pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP are agonists of VIP receptor with different binding affinities (see abstract in page 95 and Table in page 98) and it is known that VPAC1 receptor is one of VIP receptors (see the specification, page 7, third paragraph), pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP taught by Fishbein *et al.,* are VPAC1 receptor agonists as recited in claim 1. Since pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP are purified by analytical reverse-phrase HPLC (see page 96, right column, first paragraph), after the purification, pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP are in a HPLC loading

buffer. According to the definition of pharmaceutically acceptable carrier in the specification (see page 14, lines 7-19), one component such as acetonitrile in the HPLC loading buffer is considered as a pharmaceutically acceptable carrier as recited in claim 1. Furthermore, according to the definition of pharmaceutically acceptable carrier (see page 14, second paragraph), serum albumin is one of pharmaceutically acceptable carriers. Since Fishbein *et al.,* teach that the incubation buffer used for pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP (ie., VPAC1 receptor agonists) includes 0.2% BSA (see page 96, left column, fourth paragraph), BSA can also considered as a pharmaceutically acceptable carrier. Thus one or more above pseudopeptides and the HPLC loading buffer or BSA taught by Fishbein *et al.,* are components of a pharmaceutical composition as recited in claim 1. Although Fishbein *et al.,* do not show that the pharmaceutical composition comprising one or more above pseudopeptides in the HPLC loading buffer can used for the treatment and/or prevention of septic shock as recited in claim 1, the effect of the pharmaceutical composition recited in claim 1 in the treatment and/or prevention of septic shock is considered as an intended use of the pharmaceutical composition recited in claim 1. It is known that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

Therefore, Fishbein *et al.,* teach all limitations recited in claim 1.

Response to Arguments

I. In page 8, fourth paragraph bridging to page 9, first paragraph of applicant's remarks, applicant argues that "[S]ince HPLC loading buffer is a buffer as described in the specification, it is excluded from the definition of the term 'pharmaceutically acceptable carrier.' Thus, Fishbein fails to teach a pharmaceutically acceptable carrier as recited in independent claim 1" .

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection. First, the specification defines pharmaceutically acceptable carrier as "any carrier, which does not interfere with the effectiveness of the biological activity of the active ingredient and that is not toxic to the host to which is administered. For example, for parenteral administration, the above active ingredients may be formulated in unit dosage form for injection in vehicles such as saline, dextrose solution, serum albumin and Ringer's solution, liposomes" (see page 14, second paragraph). Since the specification defines saline as one of pharmaceutically acceptable carriers, which is commonly used as a buffer, and the specification does not indicate what compositions are included in the buffer, the examiner considers that one component in a buffer is a pharmaceutically acceptable carrier. Although the specification indicates that "[Besides the pharmaceutically acceptable carrier, the compositions of the invention can also comprise minor amounts of additives, such as stabilizers, excipients, buffers and preservatives" (see page 14, second paragraph), the buffer here is only considered as one or more components that have an ability to serve as a buffer. Therefore, one component in the HPLC buffer such as acetonitrile can be considered as a pharmaceutically acceptable carrier. Furthermore, according to the definition of pharmaceutically acceptable carrier, serum albumin is one of pharmaceutically acceptable carriers (see page 14, second paragraph). Since Fishbein

et al., teach that the incubation buffer used for pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP (ie., VPAC1 receptor agonists) includes 0.2% BSA (see page 96, left column, fourth paragraph), Fishbein *et al.,* disclose a pharmaceutically acceptable carrier (ie., BSA) wherein BSA is one component of the incubation buffer.

II. In page 9, second paragraph of applicant's remarks, applicant argues that "[F]ishbein does not teach HPLC loading buffer for administration of an active ingredient into a human body. Fishbein fails to teach or suggest any pharmaceutically acceptable carrier for administering an active agent into a human body. Fishbein does not teach a pharmaceutically acceptable carrier that does not interfere with the effectiveness of biological activity of the active ingredient and is not toxic to the host to which it is administered. If the examiner believes through personal knowledge that such a loading buffer would not interfere with the effectiveness of biological activity of the active ingredient and would not be toxic to the host to which it is administered, the examiner is invited to provide an affidavit supporting his contention pursuant to 37 C.F.R. §1.104(d)(2)".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, applicant does not provide an evidence to show that acetonitrile or BSA cannot serve as a pharmaceutically acceptable carrier for administering an active agent into a human body. Second, since HPLC purified pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP (ie., VPAC1 receptor agonists) taught by Fishbein *et al.,* have an inhibition effect when they are in the incubation buffer (see Figures 1 and 2, and TABLE 1), this indicates that a pharmaceutically acceptable carrier (ie., acetonitrile or

BSA) taught by Fishbein *et al.,* does not interfere with the effectiveness of the biological activity of the active ingredient (ie., one of pseudopeptides [ψ2-3]VIP, [ψ3-4]VIP, [ψ4-5]VIP, [ψ5-6]VIP, [ψ6-7]VIP, and [ψ8-9]VIP). Furthermore, applicant has no evidence to show that acetonitrile in the HPLC loading buffer is toxic to the host. Third, in view of above arguments, it appears that applicant considers that patentability of claim 1 is dependent on intended use of the pharmaceutically acceptable carrier (not toxic to the host to which is administration). However, the pharmaceutically acceptable carrier recited in claim 1 would not be patentable over a reference that teaches the same pharmaceutically acceptable carrier but lacks a teaching of the recited intended use. It is known that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

9. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Gourlet *et al.,* (Peptide, 18, 1539-1545, December 1997).

The examiner has noted that, in previous office action mailed on November 17, 2003, incorrect author's name (Xia) was used for this rejection. However, since the examiner used correct reference (Peptide, 18, 1539-1545, December 1997, including correct journal name, correct journal volume and correct initial page number of the reference) for the rejection in previous office action and applicant has received the correct reference that sent by the office (see attached interview summary on June 2, 2004), the rejection below should not considered as a new ground of rejection.

Gourlet *et al.,* teach development of high affinity selective VIP1 receptor agonists. Since two VIP receptor agonists, [R16]chicken secretin and [K15, R16, L27]VIP(1-7)/GRF(8-27), have much stronger affinity for VIP1 receptor than VIP 2 receptor (see abstract in page 1539 and right column in page 1544) and it is known that VIP1 receptor and VPAC 1 are identical, [R16]chicken secretin and [K15, R16, L27]VIP(1-7)/GRF(8-27) taught by Gourlet *et al.,* are two VPAC 1 agonists. Since [R16]chicken secretin and [K15, R16, L27]VIP(1-7)/GRF(8-27) taught by Gourlet *et al.,* are purified by a reverse-phrase chromatograph, after the purification (see page 1541, left column last paragraph), R16]chicken secretin and [K15, R16, L27]VIP(1-7)/GRF(8-27) are in a loading buffer from the reverse-phrase chromatograph. According to the definition of pharmaceutically acceptable carrier in the specification (see page 14, lines 7-19), one component of the loading buffer from the reverse-phrase chromatograph is a pharmaceutically acceptable carrier as recited in claim 1. Since Gourlet *et al.,* teach that the buffer used for the binding assay includes 1% bovine serum albumin (BSA) (see page 1541, left column, fifth paragraph), BSA can also considered as a pharmaceutically acceptable carrier. Thus [R16]chicken secretin or/ and [K15, R16, L27]VIP(1-7)/GRF(8-27), and the loading buffer from the reverse-phrase chromatograph or BSA are components of a pharmaceutical composition as recited in claim 1. Although Gourlet *et al.,* do not show that the pharmaceutical composition comprising [R16]chicken secretin or [K15, R16, L27]VIP(1-7)/GRF(8-27) in the loading buffer from the reverse-phrase chromatograph or the binding buffer can used for the treatment and/or prevention of septic shock as recited in claim 1, the effect of the pharmaceutical composition recited in claim 1 in the treatment and/or prevention of septic shock is considered as an intended use of the pharmaceutical composition recited in claim 1. It is known that a recitation of the

intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. *In re Casey*, 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

Response to Arguments

In page 9, third paragraph of applicant's remarks, applicant argues that "[T]he examiner again defines a chromatograph loading buffer as a pharmaceutically acceptable carrier. Therefore, applicant respectively submits that Xia et al. fails to teach a pharmaceutically acceptable carrier as recited in independent claim 1 for the same reasons as stated above for Fishbein".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the specification defines Pharmaceutically acceptable carrier as "any carrier, which does not interfere with the effectiveness of the biological activity of the active ingredient and that is not toxic to the host to which is administered. For example, for parenteral administration, the above active ingredients may be formulated in unit dosage form for injection in vehicles such as saline, dextrose solution, serum albumin and Ringer's solution, liposomes" (see page 14, second paragraph). Since the specification defines saline as one of pharmaceutically acceptable carriers, which is commonly used as a buffer, and the specification does not indicate what compositions are included in the buffer, the examiner considers that one component in a buffer is a pharmaceutically acceptable carrier. Although the specification indicates that "[Besides the pharmaceutically acceptable carrier, the compositions of the invention can also comprise minor amounts of additives, such as stabilizers, excipients, buffers

and preservatives" (see page 14, second paragraph), the buffer here is only considered as one or more components that have an ability to serve as a buffer. Therefore, one component in the HPLC loading buffer is considered as a pharmaceutically acceptable carrier. Furthermore, according to the definition of pharmaceutically acceptable carrier, serum albumin is one of pharmaceutically acceptable carriers. Since Gourlet *et al.,* teach that the buffer used for the binding assay includes 1% BSA (see page1541, left column, fifth paragraph), Gourlet *et al.,* disclose a pharmaceutically acceptable carrier (ie., BSA). Second, applicant does not provide an evidence to show that one component of the HPLC loading buffer or BSA cannot serve as a pharmaceutically acceptable carrier for administering an active agent into a human body. Third, since HPLC purified [R16]chicken secretin and [K15, R16, L27]VIP(1-7)/GRF(8-27) taught by Gourlet *et al.,* have an inhibition effect (see Figures 1-5), a pharmaceutically acceptable carrier (ie., a component of the HPLC loading buffer or BSA) taught by Gourlet *et al.,* does not interfere with the effectiveness of the biological activity of the active ingredient (ie., [R16]chicken secretin or [K15, R16, L27]VIP(1-7)/GRF(8-27)). Furthermore, applicant has no evidence to show that the components in the HPLC loading buffer is toxic to the host. Fourth, in view of above arguments, it appears that applicant considers that patentability of claim 1 is dependent on intended use of the pharmaceutically acceptable carrier (not toxic to the host to which is administration). However, the pharmaceutically acceptable carrier recited in claim 1 would not be patentable over a reference that teaches the same pharmaceutically acceptable carrier but lacks a teaching of the recited intended use. It is known that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior

art. If the prior art structure is capable of performing the intended use, then it meets the claim. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

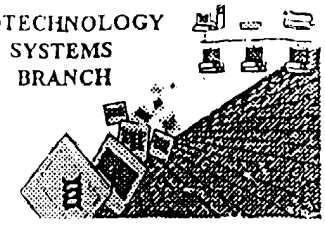
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
June 8, 2004

FRANK LU
PATENT EXAMINER

BIOTECHNOLOGY SYSTEMS BRANCH



RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/090,109B
Source: IFW16
Date Processed by STIC: 3/25/04

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
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FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 703-308-4212; FAX: 703-308-4221
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Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail
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Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm> , EFS Submission User Manual - ePAVE)
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Revised 10/08/03

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION

SERIAL NUMBER: 10/090,109

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1____ Wrapped Nucleics
Wrapped Aminos — The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."

2____ Invalid Line Length — The rules require that a line not exceed 72 characters in length. This includes white spaces.

3____ Misaligned Amino Numbering — The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.

4____ Non-ASCII — The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.

5____ Variable Length — Sequence(s)____ contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.

6____ PatentIn 2.0 "bug" — A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.

7____ Skipped Sequences (OLD RULES) — Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence:
(2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
(i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
This sequence is intentionally skipped

Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

8____ Skipped Sequences (NEW RULES) — Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence.
<210> sequence id number
<400> sequence id number
000

9____ Use of n's or Xaa's (NEW RULES) — Use of n's and/or Xaa's have been detected in the Sequence Listing.
Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

10____ Invalid <213> Response — Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence

11____ Use of <220> — Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.
(See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)

12____ PatentIn 2.0 "bug" — Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

13____ Misuse of n/Xaa — "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid

IFW16

RAW SEQUENCE LISTING DATE: 03/25/2004
PATENT APPLICATION: **US/10/090,109B** TIME: 09:24:13

Input Set : **A:\PTO.YF.txt**
Output Set: **N:\CRF4\03252004\J090109B.raw**

3 <110> APPLICANT: Perez Gomariz et al
5 <120> TITLE OF INVENTION: Method For Treating and Preventing Septic Shocic With VPAC1R, VPAC2R, and
6 PAC1R Agonists
8 <130> FILE REFERENCE: G80-016 CIP
10 <140> CURRENT APPLICATION NUMBER: 10/090,109B
11 <141> CURRENT FILING DATE: 2002-03-04
13 <150> PRIOR APPLICATION NUMBER: 09/446,352
14 <151> PRIOR FILING DATE: 2000-12-17
16 <160> NUMBER OF SEQ ID NOS: 5

ERRORED SEQUENCES

Does Not Comply
Corrected Diskette Needed
(PS. 1,4)

29 <210> SEQ ID NO: 2
30 <211> LENGTH: 43
31 <212> TYPE: DNA
32 <213> ORGANISM: artificial sequence
34 <220> FEATURE:
35 <223> OTHER INFORMATION: specific probe for TNFalpha
37 <400> SEQUENCE: 2
E--> 38 ttgacctcag cgctgagttg gtccccttc tagctggaag act
39 (43)

43 ← insert here

delete some spaces between nucleotides

RAW SEQUENCE LISTING ERROR SUMMARY DATE: 03/25/2004
PATENT APPLICATION: **US/10/090,109B** TIME: 09:24:14

Input Set : **A:\PTO.YF.txt**
Output Set: **N:\CRF4\03252004\J090109B.raw**

Invalid Line Length:
The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:1; Line(s) 5
Seq#:4; Line(s) 63

VERIFICATION SUMMARY DATE: 03/25/2004
PATENT APPLICATION: **US/10/090,109B** TIME: 09:24:14

Input Set : **A:\PTO.YF.txt**
Output Set: **N:\CRF4\03252004\J090109B.raw**

L:38 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:43 SEQ:2
L:86 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:5 after pos.:15

<210> 5
<211> 31
<212> PRT
<213> artificial sequence - please explain, Mandatory

IF <213> is Artificial/ unknown, please explain source of genetic material.

<220>
<221> ACETYLATION
<222> 1

<220>
<221> MOD_RES
<222> 17
<223> The modified residue is a Nle

<400> 5

His	Ser	Asp	Ala	Val	Phe	Thr	Glu	Asn	Tyr	Thr	Lys	Leu	Arg	Lys
				5					10					15
Gln	Xaa	Ala	Ala	Lys	Lys	Tyr	Leu	Asn	Asp	Leu	Lys	Lys	Gly	Gly
				20					25					30

Thr

Please see item # 11 on error Summary Sheet.